The functional properties of the female reproductive tract organs are dependent on establishing the correct organ-specific epithelial morphologies and differentiation. At the early stage, XX embryos possess the progenitors for both male and female reproductive tracts, also known as the Wolffian and Müllerian ducts. The two ducts are surrounded by their own distinct mesenchymes. During sexual differentiation, the XX embryo eliminates the Wolffian duct and maintains the Müllerian duct, which eventually gives rise to the oviduct, uterus, cervix, and vagina in an antero-posterior fashion. Our previous study revealed that the Wolffian duct mesenchyme was not eliminated in the XX embryo. Instead, it becomes a unique mesenchymal population localized at the mesometrial (dorsal) side of the uterus, contrary to the residence of the Müllerian duct.
mesenchyme-derived cells at the anti-mesometrial (ventral) side. It has been well-established that epithelial morphogenesis is regulated by its surrounding mesenchyme. Therefore, a subsequent question is how the two different mesenchymes contribute to the morphogenesis of the female reproductive tract. The Müllerian duct mesenchyme uniquely expresses Amhr2. To investigate the functional significance of the Müllerian duct mesenchyme in vivo, we designed the Amhr2-Cre; Rosa-DTA genetic cellular ablation model to partially remove Amhr2+ Müllerian duct mesenchyme in the female reproductive tract. After partially ablating the Amhr2+ Müllerian duct mesenchyme, the oviduct became shorter and lost its characteristic coiling. Oviductal epithelial proliferation was significantly reduced, which contributed to the defective oviductal elongation and coiling. Surprisingly, the regionalization of the oviduct into the infundibulum, ampulla, and isthmus was not affected in the ablation group, suggesting that oviductal coiling and regionalization are two uncoupled events. The uterus looked shorter in the ablation group. Histology analysis further revealed the disorganization of the lumen shape. Normally, the lumen shape of the neonatal uterus forms an ellipse with the long axis parallel to the dorso-ventral axis. In the ablation group, however, the uterine shape was irregular and the long axis of the lumen became perpendicular to the dorso-ventral axis. These results demonstrate that Amhr2+ mesenchyme is indispensable for the morphological patterning of the female reproductive tract along both the antero-posterior and dorso-ventral axes. To investigate the mechanisms underlying the morphological defects in the ablation group, we are in the process of investigating cellular events that have been implicated in the female reproductive tract patterning: cellular apoptosis, proliferation, and orientation of cell division. Taken together, our study provides a novel model to understand how the mesenchyme patterns the female reproductive tract in place. This work was supported by NIH grant R00 HD096051.

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